REUTERS HEALTH INFORMATION

Low-dose radiation for Hodgkin's lymphoma leaves kids at high risk for second cancers

February 8, 2010 (Reuters Health) -

Last Updated: 2010-02-08 19:13:21 -0400 (Reuters Health)

By Michelle Rizzo

NEW YORK (Reuters Health) - Low-dose radiation for Hodgkin's lymphoma leaves children at a significant risk for second malignancies, according to researchers at Stanford University Medical Center in California.

"Because it is now well established that radiation exposure is associated with the development of second cancers, particularly solid tumors, later in life, we wanted to find out if adult survivors treated with a lower dose radiation based protocol as children would suffer second cancers," lead author Dr. Maureen M. O'Brien told Reuters Health by email. Dr. O'Brien is now at Cincinnati Children's Hospital Medical Center in Ohio.

In a February 1 online paper in the Journal of Clinical Oncology, she and her colleagues report on 110 pediatric Hodgkin's lymphoma survivors who received chemotherapy and low-dose radiation between 1970 and 1990. The children were treated with two combined modality treatment protocols that included 6 cycles of chemotherapy in addition to 15 to 25.5 Gy involved-field radiation plus 10 Gy boosts to bulky sites.

During follow-up over a median of 20.6 years, 18 patients developed at least one second cancer, including 4 cases of leukemia, 17 solid tumors, 5 thyroid carcinomas, 6 breast carcinomas, and 4 sarcomas.

The estimated cumulative incidence of an initial second malignancy was 17% at 20 years and 29.4% at 30 years after diagnosis. "The majority of the risk is due to solid tumors with a cumulative incidence of 14.3% at 20 years...and 27.2% at 30 years," the authors write.

Among patients who developed solid tumors, the mean 5-year disease-free survival was 76%, and the mean 5-year overall survival was 85% (with a median follow-up of 5 years since the diagnosis of the initial second cancer).

All of the patients with secondary leukemias died.

The standard incidence ratio for any second cancer was 22.9, and the absolute excess risk was 93.7 cases for every 10,000 person-years.

"These results support the need for continued basic science research to better understand the genetic factors that predispose some survivors to develop second cancers while others do not, despite exposure to similar treatment," Dr. O'Brien noted.

She added that the results are a "reminder of the importance of the need for ongoing care and education of cancer survivors, with close surveillance and screening for second cancers as well as other long term effects of treatment."

J Clin Oncol 2010.

LLS asked Louis S. Constine, MD, FASTRO, Professor of Radiation Oncology and Pediatrics and Vice Chair, Department of Radiation Oncology at the James P. Wilmot Cancer Center, University of Rochester Medical Center, Rochester, NY to provide a perspective about current radiotherapy practices for children with Hodgkin lymphoma (HL).
This study shows that relatively low doses of adjuvant radiation therapy used to treat children with HL between 1970 and 1990 increased the risk for the development of other cancers. This is an important contribution because it demonstrates the ongoing risks for the occurrence of treatment-related cancers. Yet, it is reasonable to be optimistic that current therapeutic strategies will be less likely to induce secondary cancers. These treatment approaches tailor chemotherapy intensity and radiation therapy for patients, based on both risk and response of

the patient. Today, radiation doses rarely exceed a total of 21 Gy (whereas some children in the study received up to 35.5 Gy). Also, the radiation volumes have become progressively smaller to minimize effects on normal tissues. Still, the focus of treatment for children with HL is (and should be) to cure their disease while minimizing the risk for subsequent cancers or other late effects. Ongoing surveillance of survivors is critical to for prevention or early treatment of late effects, along with research into HL causes, risks and even less toxic treatment.

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September 15, 2009 (Press Releases) -

For Immediate Release
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White Plains, N.Y. (September 15 2009) - The cure rates for many cancers have improved dramatically over the past decades, but the harsh reality is that too many cancer survivors suffer serious side-effects of their curative treatments. Toxic side-effects can occur months or years after the treatments are finished, sometimes as chronic conditions, sometimes life-threatening, but always unacceptably reducing a patient's quality of life.

While research continues to seek new safe and effective drugs, what patients need now is for current therapies to be made less harmful without sacrificing their effectiveness.

In a new initiative, The Leukemia & Lymphoma Society (LLS) will invest in research designed to discover the biological mechanisms that cause late effects, and to develop and test measures to prevent or at least significantly reduce toxicities. LLS is seeking requests for proposals from scientists studying these issues. (http://www.leukemia-lymphoma.org/graphics/National/QualityofLifeResearchFundingOpportunity.pdf)

The pediatric cancer story has shown us that the goal is achievable. Years of research and clinical trials enabled survival rates to reach nearly 90% for children with acute lymphocytic leukemia. But then the medical and research community recognized that the serious late effects were severely impacting quality of life. High-dose radiation treatments, once thought critical to cures, have been eliminated for most children, significantly reducing cognitive deficits and other once common side-effects.

Now LLS has set a goal of doing for all cancer patients, regardless of age, what has been achieved for many children - survival with good quality of life.

The initiative is being led by **Anna T. Meadows, M.D.**, medical director of the Cancer Survivorship and Living Well After Cancer Program at the Children's Hospital of Philadelphia. Dr. Meadows is an internationally recognized pioneer in late effects research; she helped quantify the serious consequences of high-dose radiation and eliminate it from curative treatments for most children with leukemia and lymphoma.

"We must find the answers and test them as soon as possible," says Dr. Meadows. "We must be determined and courageous - funders, researchers, and patients alike - because survival is just the first part of the struggle to cure cancer; the quality of that survival matters."

To learn more about the LLS Quality of Life Funding Initiative, visit http://www.leukemia-lymphoma.org/graphics/National/QualityofLifeResearchFundingOpportunity.pdf

About The Leukemia & Lymphoma Society
The Leukemia & Lymphoma Society® (LLS) is the world's largest voluntary health agency dedicated to blood cancer. The LLS mission: Cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families. LLS funds lifesaving blood cancer research around the world and provides free information and support services.

Founded in 1949 and headquartered in White Plains, NY, LLS has chapters throughout the United States and Canada. To learn more, visit www.LLS.org or contact the Information Resource Center at (800) 955-4572, Monday through Friday, 9 a.m. to 6 p.m. ET. www.lls.org.

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REUTERS HEALTH INFORMATION

Risk of breast cancer after radiotherapy in childhood quantified

July 20, 2009 (Reuters Health) -

Last Updated: 2009-07-20 16:00:40 -0400 (Reuters Health)

NEW YORK (Reuters Health) - The results of a study confirm that girls who undergo radiation for cancer in childhood have an increased long-term risk of developing breast cancer, regardless of the age at exposure.

The study findings also suggest a protective effect of irradiation of the ovaries on future breast cancer risk in childhood cancer survivors.

To quantify the risk of breast cancer in relation to radiation dose and chemotherapy in survivors of childhood cancer, Dr. Peter D. Inskip of the National Cancer Institute, Bethesda, Maryland, and colleagues conducted a case-control study of new primary breast cancers in a large cohort of women who survived childhood cancer.

Case patients included 120 women diagnosed with cancer when they were younger than 21 years old, were treated between 1970 and 1986, and survived for at least 5 years. Each case patient was matched to four controls by age at diagnosis of first cancer and duration of survival.

Hodgkin's lymphoma was the initial cancer in 65.0% of cases and 40.1% of controls. Bone and soft tissue sarcomas were the next most common first cancers in case patients.

The median age at diagnosis of the first cancer was 16.0 years and the median age at diagnosis of the breast cancer was 35.9 years.

Overall, chemotherapy for the initial cancer was not associated significantly with breast cancer risk in analyses adjusted for radiation dose to the breast and ovary. However, borderline significantly elevated risks of breast cancer were evident for doxorubicin, dactinomycin, dacarbazine and carmustine.

In contrast, there was a "highly significant, linear relation between radiation dose and breast cancer risk," Dr. Inskip and colleagues report in the July 20th issue of the Journal of Clinical Oncology.

Women who underwent local breast radiation doses of 40 Gy had an 11.8-fold increased risk of breast cancer compared with nonirradiated patients (p for trend < 0.0001).

However, according to the researchers, the risk associated with breast irradiation was "sharply reduced" in women whose treatment of the initial cancer included a sterilizing radiation dose to the ovaries of 5 Gy or more ($p = 0.002$). A breast dose of 40 Gy was associated with only a 3.4-fold risk of breast cancer in this subgroup of women, they found.

"These data point to an important role of hormonal stimulation on radiation-related breast cancer," the authors write. "The cohort," they point out, "is still relatively young, and the largest part of the radiation-related absolute excess occurrence of breast cancer may yet be seen."

J Clin Oncol 2009;27.

There are several types of studies to improve the care of Hodgkin lymphoma, including studies to address causes, risk factors and quality of life issues. Examples of the questions that studies seek to answer are shown in Table 6.

Table 6. Study Questions for Hodgkin Lymphoma Clinical Trials

- How can we lower the risk of long-term and late effects of treatment?
- What can we learn about biomarkers and genetic causes of Hodgkin lymphoma (familial clustering) that may lead to a better understanding of causes, risk factors and less toxic treatments?
- How can we improve the quality of life for the many survivors of Hodgkin lymphoma?
- Can we develop more effective and less toxic treatments for patients with advanced, relapsed or refractory Hodgkin lymphoma?
- Can new approaches to stem cell transplantation make this therapy safer, especially for older and sicker patients?
- What is the role of vaccine therapy in the treatment of Hodgkin lymphoma?

The Information Resource Center at LLS, (800) 955-4572, offers guidance on how patients can work with their physicians to find out if a specific clinical trial is an appropriate treatment option. Information Specialists will conduct individualized clinical trial searches for patients, family members and healthcare professionals. This service is also available on the Web site at www.LLS.org.

Table 6. Many different questions are being addressed in ongoing clinical trials. Patient participation is needed. For more information speak to your physician or contact an Information Specialist at LLS.